



Docket Number: 660005.98757

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Michael C. Barney *et al.*
Serial No.: 09/664,519
Filing Date: September 18, 2000
For: USE OF HOP ACIDS TO INHIBIT GROWTH OF
STAPHYLOCOCCUS AUREUS AND PREVENT
TOXIC SHOCK SYNDROME
Examiner: Chih Min Kam
Group Art Unit: 1653

DECLARATION

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

1. I am the first named inventor for the above-identified patent application.
2. I read the comments in the Advisory Action of October 16, 2003 regarding U.S. Patent No. 5,082,975 to Todd *et al.* showing that "HHC [hexahydrocolupulone] at high concentration (50-200 ppm) inhibits the growth of certain lactobacilli." The Advisory Action concludes that "therefore, if the concentration of HHC is reduced to a lower concentration such as in the range of 0.2-25 ppm, the inhibition of the growth of lactobacilli would be lessened, which allows the growth of lactobacilli."
3. Without the benefit of the experiments that I or others working under my supervision conducted and that are reported in the above-identified patent application, it

would have been impossible to predict the effects of a lower concentration of HHC (such as in the range of 0.2-25 ppm) on the growth of lactobacilli.

4. Hop acids such as hexahydrocolupulone inhibit the growth of bacteria by disrupting ion transport across bacterial cell membranes. However, it is very difficult to predict the number of molecules needed to disrupt ion transport across particular bacterial cell membranes.

5. Todd *et al.* show that hexahydrocolupulone inhibits the growth of certain lactobacilli in milk (pH 6.4-6.8) at 50-200 ppm and therefore, ion transport across certain lactobacilli bacterial cell membranes is disrupted at these levels in milk. However, these experiments cannot be used to predict the minimum number of molecules needed to disrupt ion transport across lactobacilli bacterial cell membranes, particularly at the vaginal pH of 4.5-5.0.

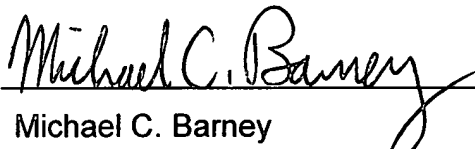
6. The present application illustrates this concept. In particular, attention is directed to the far right hand column of Table 1 of the present application. When testing hexahydro beta acid at concentrations of 50 and 100 ppm for *Staphylococcus aureus* inhibition, no growth of *Staphylococcus aureus* was observed. Also, at concentrations of 0.2 to 25 ppm, no growth of *Staphylococcus aureus* was observed. Thus, the activity at 50 and 100 ppm in no way provided a prediction of the activity at 0.2 to 25 ppm. In other words, lowering the concentration did not automatically lessen the inhibitory action.

7. In summary, the response of all organisms to hop acids is unpredictable as all organisms are different. Thus, the activity of hop acids on lactobacilli below the

50 ppm level reported in Todd *et al.* at vaginal pH of 4.5-5.0 could not be predicted from Todd *et al.*

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

Dated: November 20, 2003


Michael C. Barney